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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 213/00 | A2

(11) International Publication Number: WO 99/02497

(43) International Publication Date: 21 January 1999 (21.01.99)

(21) International Application Number: PCT/EP98/04266

(22) International Filing Date: 9 July 1998 (09.07.98)

(30) Priority Data:

08/891,691	11 July 1997 (11.07.97)	US
08/890,689	11 July 1997 (11.07.97)	US

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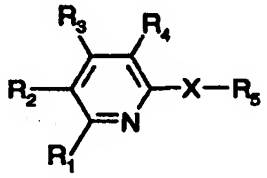
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: PYRIDINE DERIVATIVES



(I)

(57) Abstract

Compounds of the formula (I), wherein X and R_1 to R_5 are as defined in the description, are useful for treating disorders mediated full or in part by mGluR5.

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Pyridine derivatives

The invention relates to the use of 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines for modulating the activity of mGluRs and for treating mGluR5 mediated diseases, to pharmaceutical compositions for use in such therapy, as well as to novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines.

It has been found that 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines including the pharmaceutically acceptable salts (hereinafter agents of the invention) are useful as modulators of mGluRs. Modulation of mGluRs can be demonstrated in a variety of ways, inter alia, in binding assays and functional assays such as second messenger assays or measurement of changes in intracellular calcium concentrations. For example, measurement of the inositol phosphate turnover in recombinant cell lines expressing hmGluR5a showed, for selected agents of the invention, IC_{50} values of about 1nM to about 50μM.

In particular, the agents of the invention have valuable pharmacological properties. For example, they exhibit a marked and selective modulating, especially antagonistic, action at human metabotropic glutamate receptors (mGluRs). This can be determined in vitro for example at recombinant human metabotropic glutamate receptors, especially PLC-coupled subtypes thereof such as mGluR5, using different procedures like, for example, measurement of the inhibition of the agonist induced elevation of intracellular Ca^{2+} concentration in accordance with L. P. Daggett et al. Neuropharm. Vol. 34, pages 871-886 (1995), P. J. Flor et al., J. Neurochem. Vol. 67, pages 58-63 (1996) or by determination to what extent the agonist induced elevation of the inositol phosphate turnover is inhibited as described by T. Knoepfel et al. Eur. J. Pharmacol. Vol. 288, pages 389-392 (1994), L. P. Daggett et al., Neuropharm. Vol. 67, pages 58-63 (1996) references cited therein. Isolation and expression of human mGluR subtypes are described in US-Patent No. 5,521,297. Selected agents of the invention showed IC_{50} values for the inhibition of the quisqualate-induced inositol phosphate turnover, measured in recombinant cells expressing hmGluR5a of about 1nM to about 50μM.

Accordingly the invention relates to agents of the invention for use in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

Disorders associated with irregularities of the glutamatergic signal transmission are for example epilepsy, cerebral ischemias, especially acute ischemias, ischemic diseases of the eye, muscle spasms such as local or general spasticity and, in particular, convulsions or pain.

Nervous system disorders mediated full or in part by mGluR5 are for example acute, traumatic and chronic degenerative processes of the nervous system, such as Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis and multiple sclerosis, psychiatric diseases such as schizophrenia and anxiety, depression and pain.

The invention also relates to the use of agents of the invention, in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by Group I mGluRs.

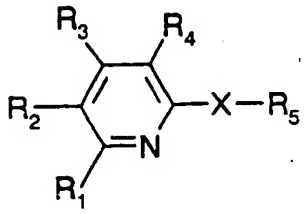
Furthermore the invention relates to the use of agents of the invention for the manufacture of a pharmaceutical composition designed for the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by Group I mGluRs.

In a further aspect the invention relates to a method of treating disorders mediated full or in part by group I mGluRs (preferentially mGluR5) which method comprises administering to a warm-blooded organism in need of such treatment a therapeutically effective amount of an agent of the invention.

In still a further aspect, the invention relates to novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines and their salts, and to a process for preparing them.

Moreover the invention relates to a pharmaceutical composition comprising as pharmaceutical active ingredient, together with customary pharmaceutical excipients, a novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- or 2-heteroarylazo-pyridine or a pharmaceutically acceptable salt thereof.

Agents of the invention are for example compounds of formula I



(I),

wherein

R_1 denotes hydrogen, lower alkyl, hydroxy-lower alkyl lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R_2 denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 represents hydrogen, lower alkyl, carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy- lower alkyl, di- lower alkyl- aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy,

X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and

R_5 denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-lower alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or

trifluoromethyl-substituted phenyl-low r alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted,
customary photoaffinity ligands and customary radioactive markers, inclusive of their N-oxides and their pharmaceutically acceptable salts.

Compounds of formula I having basic groups may form acid addition salts, and compounds of the formula I having acidic groups may form salts with bases. Compounds of formula I having basic groups and in addition having at least one acidic group, may also form internal salts.

Also included are both total and partial salts, that is to say salts with 1, 2 or 3, preferably 2, equivalents of base per mole of acid of formula I, or salts with 1, 2 or 3 equivalents, preferably 1 equivalent, of acid per mole of base of formula I.

For the purposes of isolation or purification it is also possible to use pharmaceutically unacceptable salts. Only the pharmaceutically acceptable, non-toxic salts are used therapeutically and they are therefore preferred.

Halo in the present description denotes fluorine, chlorine, bromine or iodine.

When X represents an alkenylene group, configuration trans is preferred.

Preferred compounds of formula I are those wherein

X represents an optionally halo-substituted (C_{2-4})alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms,

R_1 is hydrogen, (C_{1-4}) alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, cyano, ethynyl, carboxy, (C_{1-4})alkoxycarbonyl, di(C_{1-4})alkylamino, (C_{1-6})alkylaminocarbonyl, trifluoromethylphenylaminocarbonyl,

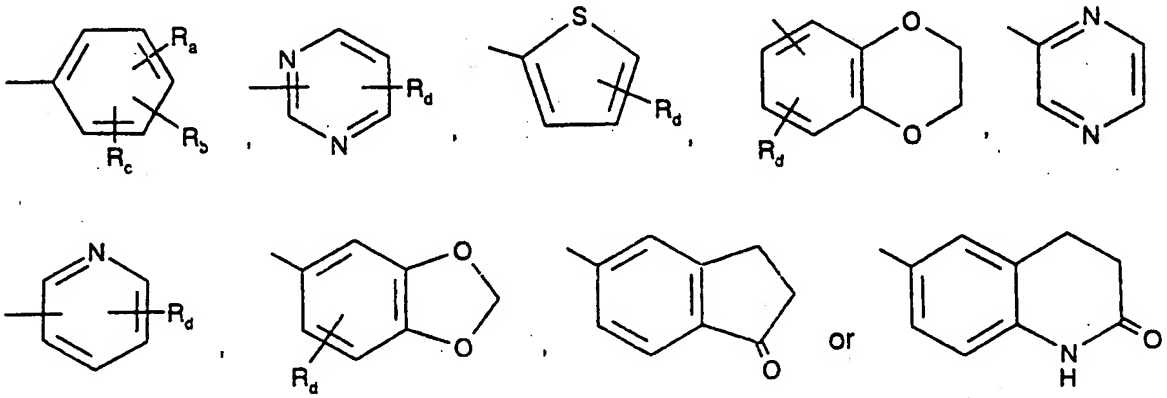
R_2 is hydrogen, hydroxy, (C_{1-4}) alkyl, hydroxy (C_{1-4}) alkyl, (C_{1-4}) alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4}) alkoxycarbonyl, di(C_{1-4})alkylamino(C_{1-4})alkanoyl,

di(C_{1-4})alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 is hydrogen, (C_{1-4}) alkyl, carboxy, (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbamoyl, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 is hydrogen, hydroxy, (C_{1-4})alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl, carboxy (C_{1-4})alkylcarbonyl, (C_{1-4})alkoxycarbonyl(C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylamino(C_{1-4})alkoxy, m-hydroxy-p-azidophenylcarbonylamino(C_{1-4})alkoxy, and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, hydroxy, halogen, nitro, cyano, carboxy, (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, (C_{1-4})alkoxycarbonyl, (C_{2-7})alkanoyl, (C_{2-5})alkanoyloxy, (C_{2-5})alkanoyloxy(C_{1-4})alkyl, trifluoromethyl, trifluoromethoxy, trimethylsilylethynyl, (C_{2-5})alkynyl, amino, azido, amino (C_{1-4})alkoxy, (C_{2-5})alkanoylamino(C_{1-4})alkoxy, (C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino (C_{1-4})alkoxy, (C_{1-4})alkylamino, di(C_{1-4})alkylamino, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, (C_{2-5})alkanoylamino, benzylcarbonylamino, (C_{1-4})alkylaminocarbonylamino, (C_{1-4})alkoxycarbonyl-aminocarbonylamino or (C_{1-4})alkylsulfonyl,

R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C_{1-4})alkyl, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxy or cyano, and

R_d is hydrogen, halogen or (C_{1-4})alkyl.

More preferred compounds of formula I are those wherein X is as defined above and

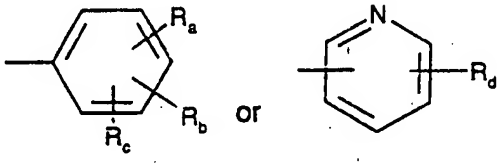
R_1 is hydrogen, (C_{1-4}) alkyl, (C_{1-4})alkoxy, cyano, ethynyl or di(C_{1-4})alkylamino,

R_2 is hydrogen, hydroxy, carboxy, (C_{1-4}) alkoxycarbonyl, di(C_{1-4})alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 is as defined above,

R_4 is hydrogen, hydroxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino (C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl or hydroxy(C_{1-4})alkyl, and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, halogen, nitro, cyano, (C_{1-4})alkyl, (C_{1-4})alkoxy, trifluoromethyl, trifluoromethoxy or (C_{2-5})alkynyl, and

R_c and R_d are as defined above.

The agents of the invention include, for example, the compounds described in the examples hereinafter.

The usefulness of the agents of the invention in the treatment of the above-mentioned disorders could be confirmed in a range of standard tests including those indicated below:

At doses of about 10 to 100 mg/kg i.p. or p.o. with pretreatment times of 15 min. to 8 hours, the agents of the invention show anticonvulsive activity in the electroshock induced convulsion model [cf. E.A. Swinyard, J. Pharm. Assoc. Scient. Ed. 38, 201 (1949) and J. Pharmacol. Exptl. Therap. 106, 319 (1952)].

At doses of about 4 to about 40 mg/kg p.o., the agents of the invention show reversal of Freund complete adjuvant (FCA) induced hyperalgesia [cf. J. Donnerer et al., Neuroscience 49, 693-698 (1992) and C.J. Woolf, Neuroscience 62, 327-331 (1994)].

For all the above mentioned indications, the appropriate dosage will of course vary depending upon, for example, the compound employed, the host, the mode of administration and the nature and severity of the condition being treated. However, in general, satisfactory results in animals are indicated to be obtained at a daily dosage of from about 0.5 to about 100 mg/kg animal body weight. In larger mammals, for example humans, an indicated daily dosage is in the range from about 5 to 1500 mg, preferably about 10 to about 1000 mg of the compound conveniently administered in divided doses up to 4 times a day or in sustained release form.

Preferred compounds for the above mentioned indications include (3-{2-[2-trans-(3,5-dichlorophenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethylamine (A), 2-methyl-6-styryl-pyridine (B), 2-(3-fluoro-phenylethynyl)-6-methyl-pyridine (C) and 2-(4-ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine (D). It has for example been determined that in the above-mentioned electroshock induced convulsion model, compounds A and B show anticonvulsive activity with ED_{50}s of 30 and 35 mg/kg i.p. respectively (pretreatment times: 4 hours and 15 min. respectively) and that in the above-mentioned FCA induced hyperalgesia model, compounds C and D show reversal of the hyperalgesia with ED_{50}s of 4.2 and 19 mg/kg p.o. respectively (post-treatment time: 3 hours).

As indicated above, the agents of the invention include novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines and their salts, hereinafter referred to as "compounds of the invention".

Compounds of the invention include compounds of formula I as defined above, and their salts, wherein X and R_1 to R_5 are as defined above, provided that when R_3 is hydrogen, a) in compounds of the formula I in which R_1, R_2 and R_4 are hydrogen, R_5 is different from phenyl, monohalophenyl, 2,4- and 3,4-dichlorophenyl, 3- and 4-trifluoromethylphenyl, methylphenyl, 3,4- and 2,5-dimethylphenyl, 4-isopropylphenyl, 3,5-di-tert.-butylphenyl, methoxyphenyl, 3,4-dimethoxyphenyl, 2,4,5- and 3,4,5-trimethoxyphenyl, hydroxyphenyl, 3,5-dihydroxyphenyl, 4-hydroxy-3,5-dimethyl-phenyl, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-phenyl, 4-hydroxy-(3-methyl-5-tert.-butyl-, 2- and 4-acetylaminophenyl, 3,5-diisopropyl- and 3,5-di-tert.-butyl)phenyl, 4-carboxy- and 4-ethoxycarbonylphenyl, 4-cyanophenyl, 3-methoxycarbonylphenyl, 3-carboxy-5-methoxy-phenyl, 2-pyridinyl, 5-chloro-2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene, or R_5 is different from phenyl, 4-methylphenyl, 4-methoxyphenyl, 4-bromophenyl and 2- and 4-chlorophenyl when

X denotes 1,2-propylene attached to R_5 in 2-position, or R_5 is different from phenyl, 2- and 4-chlorophenyl and 3-methoxyphenyl when X denotes 1,2-propylene attached to R_5 in 1-position, or R_5 is different from 4-methoxyphenyl when X denotes 2,3-but-2-enylene or 1,2-but-1-enylene attached to R_5 in 2-position, or R_5 is different from 4-methoxyphenyl and 4-isopropyphenyl when X denotes 2,3-pent-2-enylene attached to R_5 in 3-position, or R_5 is different from phenyl, 4-methylphenyl, methoxyphenyl and 4-hydroxyphenyl when X denotes 3,4-hex-3-enylene;

b) in compounds of the formula I in which R_1 is methyl and R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 4-cyanophenyl, , 2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene;

c) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is carboxy, R_5 is different from phenyl, 3-methylphenyl, 4-methoxyphenyl and 4-bromophenyl when X denotes ethenylene;

d) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is methyl, R_5 is different from phenyl, 3-methoxy-, 4-methoxy- and 3,4-dimethoxyphenyl, 2-chloro- and 2,4-dichlorophenyl and 6-methyl-pyrid-2yl when X denotes ethenylene or R_5 is different from phenyl when X is 1,2-prop-1-enylene attached to R_5 in 2-position;

e) in compounds of the formula I wherein R_1 and R_2 are hydrogen and R_4 is 2-dimethyl-aminoethoxycarbonyl or 3-dimethylaminopropyloxycarbonyl, R_5 is different from 4-methoxy-phenyl when X denotes ethenylene;

f) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is 2-dimethoxy-ethoxy, R_5 is different from phenyl, 4-methylphenyl and 4-methoxycarbonylphenyl when X denotes ethenylene;

g) R_5 is different from phenyl when R_1 and R_2 are hydrogen and R_4 is hydroxy or ethoxy-carbonyl, or when R_1 and R_2 are hydrogen and R_4 is hydroxy, or when R_1 is methyl, R_2 is hydrogen and R_4 is methoxy, or R_1 is but-1-enyl, R_2 is hydrogen and R_4 is hydrogen, or R_1 is hydrogen and R_4 is 2-dimethoxyethoxy, and X is, in each case, ethenylene,

and provided that, when R_3 is hydrogen and X is ethynylene,

a') R_5 is different from phenyl, 2- and 4-nitrophenyl, 4-aminophenyl, 4-chlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 4-ethoxycarbonylphenyl, 5-formyl-2-methoxy-phenyl, 5-carboxy-2-methyo-phenyl and pyridyl when R_1, R_2 and R_4 are hydrogen;

b') in compounds of the formula I in which R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl. 6-methylpyridin-2-yl and 2-methoxyphenyl when R_1 is methyl, R_5 is different form 6-bromopyridin-2-yl when R_1 is bromo, and R_5 is different form 6-hexyloxypyridin-2-yl when R_1 denotes hexyloxy;

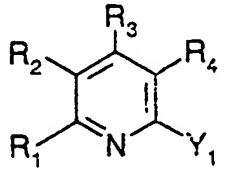
c') in compounds of the formula I wherein R_1 and R_4 are hydrogen, R_5 is different from phenyl, 4-aminophenyl and 4-propylphenyl when R_2 is methyl, R_5 is different from phenyl, 4-cyanophenyl and 4-pentylphenyl when R_2 is ethyl, R_5 is different form 3-cyano-4-ethoxy-phenyland 3-bromo-4-methoxy-phenyl when R_2 is butyl, R_5 is different from 4-methoxy-phenyl and 4 butyloxyphenyl when R_2 is pentyl, R_5 is different form 4-ter.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl, 4-tert.-butyl-3-hydroxy-phenyl,and 4-hexyloxyphenyl when R_2 is carboxy, R_5 is different from phenyl when R_2 is methoxycarbonyl or methylcarbamoyl, R_4 is different form 3-tert.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl and 4-(4-methylpentyl)phenyl when R_2 is ethoxycarbonyl, and R_5 is different from 4-pentyloxyphenyl when R_2 is 2-methylbutyloxycarbonyl;
d') in compounds of the formula I wherein R_1 and R_2 are hydrogen, R_5 is different from phenyl when R_4 is hydroxy, methyl, ethyl, carboxy, methoxycarbonyl or carbamoyl.

Preferred compounds of the invention are as indicated above for the agents of the invention.

The compounds of the invention can be prepared in analogy to the synthesis of known compounds of formula I.

Thus the compounds of the invention which are of formula I can be prepared for example by a process which comprises

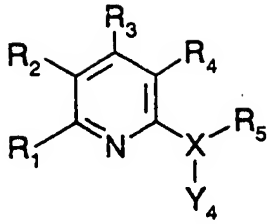
a) reacting a compound of the formula II



(II)

with a compound of the formula $Y_2 — R_5$ (III), in which either one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents lower alkyl or triarylphosphoranylidenemethyl, or one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group $Y_3 — X$- in which Y_3 is hydrogen or a metallic group, and R_1, R_2, R_3, R_4 and R_5 have the meanings indicated hereinbefore and functional groups R_1, R_2, R_3 and R_4 as well as functional substituents of R_5 may be temporarily protected, or

b) eliminating $H — Y_4$ from a compound of the formula IV



(IV),

in which Y_4 denotes an electrofugal group and R_1, R_2, R_3, R_4, X and R_5 have the meanings indicated hereinbefore and functional groups R_1, R_2, R_3 and R_4 as well as functional substituents of R_5 may temporarily be protected, removing any temporary protecting groups

and, if desired, converting a compound of formula I obtainable by the above-defined processes into a different compound of formula I, resolving a mixture of isomers that may be obtained into the individual isomers and/or converting a compound of formula I having at least one salt-forming group obtainable by the above-defined processes into a salt, or converting a salt obtainable by the above-defined processes into the corresponding free compound or into a different salt.

A lower alkanoyl Y_2 or, more preferably, Y_1 group is, for example, a C_1-C_3alkanoyl group, such as formyl, acetyl or propionyl, especially formyl. A lower alkyl group Y_1 or, more preferably, Y_2 is, for example, a C_1-C_3alkyl group, such as methyl, ethyl or propyl, especially methyl. Triarylphosphoranylidenemethyl Y_2 or, more preferably, Y_1 is, for example, triphenylphosphoranylidenemethyl.

When one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group of the formula Y_3–X- in which Y_3 denotes hydrogen, the condensation is preferably performed according to the Heck coupling method, for example, in the presence of copper or of a copper catalyst or of a noble metal/phosphine catalyst, such as Palladium or a PdII salt in the presence of triaryl phosphine, for example, Palladium acetate, and of triphenylphosphine, or in the presence of bis-triphenylphosphine-palladium dichloride, preferably in the presence of a tri-lower alkyl amine, for example, trimethylamine, advantageously in the presence of Cu^{I}-I, in a polar organic solvent such as N,N-di-lower alkyl-alkanoic acid amide, for example, dimethylformamide, a di-lower alkyl sulfoxide, for example, dimethylsulfoxide, or dioxan, at temperatures from appropriately 15° C to appropriately 120° C, preferably at the boil.

When one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group of the formula Y_3–X- in which Y_3 denotes a metallic group such as a

halo-magnesium group, the reaction is preferably performed according to Grignard method, wherein the metallic intermediate is preferably formed *in situ*.

When one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents lower alkyl, the intermolecular condensation of compounds of the formulae II and III is preferably performed according to the Shaw and Wagstaff method or one of its many modifications.

When one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents triarylphosphoranylidenemethyl , the condensation is preferably performed according to the well known Wittig olefin-building method, preferably by forming the phosphoranylidene component from a corresponding triarylphosphonium halide *in situ*, for example, by reacting the latter with a metal base, such as an alkalimetal hydride, such as sodium hydride, or with a metal-organic base, such as a lower alkyl metal compound, such as butyllithium, or with an alkali metal alkanolate, for example, potassium tertiary butoxide, preferably in an inert organic solvent, such as an aromatic or arylaliphatic hydrocarbon, for example, benzene or toluene, at appropriately -10° C to appropriately 39° C, preferably first at 0° to 10° C and then at ambient temperature.

Electrofugal groups Y_4 are, for example, esterified hydroxy groups, such as hydroxy groups esterified with an organic acid, for example, lower alkanoyloxy or hydroxy groups esterified with an anorganic acid, for example, halo groups, or tertiary amino groups, such as tri-lower alkylamino groups, for example, trimethylamino, or lower-alkyleneamino, lower azaalkyleneamino, lower-oxyalkyleneamino or lower thiaalkyleneamino groups, such as pyrrolidino, piperidino, morpholino or thiomorpholino, or corresponding quaternary ammonium groups.

The protection of functional groups by such protecting groups, the protecting groups themselves and the reactions for their removal are described, for example, in standard works.

The elimination of H —Y_4 from compounds of formula IV can be performed in a customary manner. Thus, water or lower alkanoic acids may be eliminated by means of azeotropic distillation, for example, in toluene, advantageously under mild-acidic conditions. Hydrogen halides may be removed under basic conditions such as reaction with an alkalimetal alkanolate, preferably in the corresponding lower alkanol as a solvent or co-solvent, or by heating in the presence of a tertiary amine, such as a tri-lower alkylamine.

The starting materials for the above described reactions are generally known. Novel starting materials can be obtained in manner analogous to the methods for the preparation of known starting materials.

Compounds of formula I obtainable in accordance with the process can be converted into different compounds of formula I in customary manner, for example a free carboxy group may be esterified or amidated, an esterified or amidated carboxy group may be converted into a free carboxy group, an esterified carboxy group can be converted into an unsubstituted or substituted carbamoyl group, a free amino group can be acylated or alkylated, and a free hydroxy can be acylated.

Also, compounds of the formula I can be oxidized by customary methods such as reaction with an organic peroxy acid, yielding the corresponding pyridine-N-oxide derivatives.

Salts of compounds of formula I can also be converted in a manner known *per se* into the free compounds, for example by treatment with a base or with an acid.

Resulting salts can be converted into different salts in a manner known *per se*.

The compounds of formula I, including their salts, may also be obtained in the form of hydrates or may include the solvent used for crystallization.

As a result of the close relationship between the novel compounds in free form and in the form of their salts, hereinbefore and hereinafter any reference to the free compounds and their salts is to be understood as including the free compounds, as well as the corresponding salts.

In a compound of formula I the configuration at individual chirality centers can be selectively reversed. For example, the configuration of asymmetric carbon atoms that carry nucleophilic substituents, such as amino or hydroxy, can be reversed by second order nucleophilic substitution, optionally after conversion of the bonded nucleophilic substituent into a suitable nucleofugal leaving group and reaction with a reagent introducing the original substituent, or the configuration at carbon atoms having hydroxy groups can be reversed by oxidation and reduction, analogously to European Patent Application EP-A-0 236 734.

The invention relates also to pharmaceutical compositions comprising compounds of formula I.

The pharmacologically acceptable compounds of the present invention may be used, for example, in the preparation of pharmaceutical compositions that comprise an effective amount of the active ingredient together or in a mixture with a significant amount of inorganic or organic, solid or liquid, pharmaceutically acceptable carriers.

The pharmaceutical compositions according to the invention are compositions for enteral, such as nasal, rectal or oral, or parenteral, such as intramuscular or intravenous, administration to warm-blooded animals (human beings and animals) that comprise an effective dose of the pharmacological active ingredient alone or together with a significant amount of a pharmaceutically acceptable carrier. The dose of the active ingredient depends on the species of warm-blooded animal, body weight, age and individual condition, individual pharmacokinetic data, the disease to be treated and the mode of administration.

The pharmaceutical compositions comprise from approximately 1% to approximately 95%, preferably from approximately 20% to approximately 90%, active ingredient. Pharmaceutical compositions according to the invention may be, for example, in unit dose form, such as in the form of ampoules, vials, suppositories, dragées, tablets or capsules.

The pharmaceutical compositions of the present invention are prepared in a manner known *per se*, for example by means of conventional dissolving, lyophilizing, mixing, granulating or confectioning processes.

The doses to be administered to warm-blooded animals, for example human beings, of, for example, approximately 70 kg body weight, especially the doses effective in disorders caused by or associated with irregularities of the glutamatergic signal transmission, are from approximately 3 mg to approximately 3 g, preferably from approximately 10 mg to approximately 1 g, for example approximately from 20 mg to 500 mg, per person per day, divided preferably into 1 to 4 single doses which may, for example, be of the same size. Usually, children receive about half of the adult dose. The dose necessary for each individual can be monitored, for example by measuring the serum concentration of the active ingredient, and adjusted to an optimum level.

The following non-limiting Examples serve to illustrate the invention; temperatures are given in degrees Celsius, pressures in mbar.

EXAMPLE 1

3-[2-(6-Methylpyridin-2-yl)-vinyl]-benzonitrile

A solution of 2,6-dimethyl pyridine (4.2ml, 36.28 mMol), 3-cyanobenzaldehyde (4.95g, 37.74 mMol) in acetic anhydride (6.85 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 400g). The column is first eluted with toluene (400 ml) and then with toluene/ethyl acetate 95:5. The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/hexane and 3.18 g of white crystals are isolated. (melting point: 91-92°).

EXAMPLE 2:

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), 2-cyanobenzaldehyde (6.81 g, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 400g). The column is first eluted with toluene (400 ml) and then with toluene/ethyl acetate 95:5. The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and white crystals are isolated. (melting point: 113-114°).

EXAMPLE 3

2-Methyl-6-[2-(pyridin-4-yl)-vinyl]-pyridine

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), pyridine-4-carbaldehyde (4.9 ml, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 900g). The column is first eluted with toluene/acetone 4:1 (5 L), then with toluene/acetone 3:1 (5 L) and finally with toluene/acetone 2:1 (15 L). The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and 0.956 g of white crystals are isolated. (melting point: 72-73°C).

EXAMPLE 4

2-Methyl-6-[2-(pyridin-3-yl)-vinyl]-pyridine

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), pyridine-3-carbaldehyde (4.9 ml, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 10 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 900g). The column is first eluted with toluene/acetone 9:1 (7 L), then with toluene/acetone 4:1 (5 L) and finally with toluene/acetone 2:1 (5 L). The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and 4.28 g of a colorless oil which solidify upon standing at 6-8°C.

EXAMPLE 5

2-[2-(3-Bromophenyl)ethynyl]-6-methyl-pyridine

1.2 g (2.8 mMol) of 2-[1,2-dibromo-2-(3-bromophenyl)-ethyl]-6-methyl-pyridine are dissolved in 10 ml of ethanol. 0.9 g (16.1 mMol) of potassium hydroxide (powder) are added, and the resulting suspension is heated under reflux for 4 hours. The suspension is then cooled to room temperature, poured into 100 ml of brine and extracted thrice with 30 ml each of *t*-butyl methyl ether. The combined organic phases are washed with 30 ml of brine, dried over Sodium sulfate, filtrated and evaporated *in vacuo*. 0.720 g of the title compound are obtained as a colorless oil crystallizing on standing; melting point 60-61°.

The starting material can be obtained as follows:

a) 2-[2-(3-Bromophenyl)-vinyl]-6-methyl-pyridine

A solution of 24 ml (200 mMol) of 2,6-dimethyl pyridine and 25.6 ml (207 mMol) of 3-bromobenzaldehyde in 38 ml of acetic anhydride is heated under reflux for 7.5 hours. The acetic anhydride is then evaporated *in vacuo*, and the residue is dissolved in 500 ml of 4N hydrochloric acid and twice extracted with 200 ml each of hexane. The water phase is then extracted four times with 300 ml each of tert.-butyl methyl ether. The combined organic phases are washed twice with 300 ml each of a saturated solution of $NaHCO_3$ in water, then once with 300 ml of brine (300 ml), dried over sodium sulfate, filtrated and evaporated *in vacuo* yielding 4.2 g of the title compound as colorless crystals of melting point 58-59°.

b) 2-[1,2-dibromo-2-(3-bromophenyl)-ethyl]-6-methyl-pyridine

1 g (3.6 mMol) of 2-(3-Bromo-phenylethynyl)-6-methyl-pyridine are dissolved in 5 ml of carbon tetrachloride, and the solution is heated to 55-60°. A solution of 0.23 ml (4.4 mMol) of bromine Br_2 in 1 ml of carbon tetrachloride is added dropwise. The reaction mixture is maintained at 55-60° for 30 minutes and then cooled to room temperature. The resulting precipitate is collected by filtration and dried *in vacuo*. 1.3 g of the title compound in form of yellow crystals of melting point 164-166are isolated.

EXAMPLE 6

3-[2-(6-Methylpyridin-2-yl)ethynyl]-benzonitrile

A mixture of 1 g (8.54 mMol) 2-ethynyl-6-methyl-pyridine (prepared in analogy to D. E. Ames et al., Synthesis, 1981, p. 364-5), 2.3 g (12.8 mMol) 3-bromo-benzonitrile, 0.47 g (0.7 mMol) bis-(triphenylphosphine)-palladium-II-chloride, 80 mg (0.41 mMol) cuprous iodide and 1.53 ml (15 mMol) triethylamine in 10 ml dimethylformamide is stirred for 3 hours at 90° C. The reaction mixture is cooled to ambient temperature, poured into water and extracted with dichloromethane. The organic layer is dried over sodium sulfate, filtered, evaporated to dryness and the residue is purified by chromatography on silica gel with hexane/ethyl acetate (4:1) as eluant. Crystallization from hexane of the obtained product affords 0.53 g (28.4 %) of the title compound as brown crystals, melting point 120-3° C.

EXAMPLE 7

In analogous manner to Example 1 (when X is alkenylene) or Example 5 (when X is alkynylene), the following compounds of formula I can be prepared:

Compound of formula I	Melting point (°C)
2-Styryl-pyridin-3-ol	249-252
2-Methyl-6-[2-(3-nitro-phenyl)-vinyl]-pyridine	100-101
2-[2-(2-Chloro-phenyl)-vinyl]-pyridine	colorless oil
2-Methyl-6-styryl-pyridine	40-42
Acetic acid 6-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester	75-77
6-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol	168-171
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester	99-102

2-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol	232-234
6-Methyl-2-styryl-pyridin-3-ol	261 dec
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester	92-94
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol	232-234
(Z)-6-Methyl-2-styryl-pyridin-3-ol	145-148
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridine	51-52
2-[2-(2-Fluoro-phenyl)-vinyl]-pyridine	69-70
2-[2-(2-Nitro-phenyl)-vinyl]-pyridine	97-99
Acetic acid 2-[2-(4-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester	102-103
Acetic acid 6-[2-(4-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester	130-131
2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol	275-278 dec
6-[2-(4-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol	265-270 dec
Acetic acid 6-methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester	139-140
6-Methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol	190-195 dec
Acetic acid 2-methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester	99-100
2-Methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol	230-233 dec
Acetic acid 2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester	97-99
Acetic acid 6-[2-(3-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester	112-114
2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol	232-235
6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol	230-232
(Z)-(6-Styryl-pyridin-2-yl)-methanol	69-70
(E)-(6-Styryl-pyridin-2-yl)-methanol	58-60
2,2'-(1,2-Ethenediyl)bis[6-methyl]-pyridine	108-110
Dimethyl-[3-(6-methyl-2-styryl-pyridin-3-yloxy)-propyl]-amine;hydrochloride salt	136-139
(E)-6-[2-(2-Pyridyl)vinyl]-2-picoline	56-57
2-Methyl-6-styryl-pyridine 1-oxide	102-103
2-Styryl-pyridine 1-oxide	156-159
(E)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol	240-242
(Z)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol; HCl salt	225-228
6-Styryl-pyridine-2-carbonitrile	92-93
2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridine	light yell. oil
3-Methoxy-6-methyl-2-styryl-pyridine	light yell. oil
6-Styryl-pyridine-2-carboxylic acid amide	141-142
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile	113-114

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile	91-92
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile	131-132
6-Styryl-pyridine-2-carboxylic acid; HCl Salt	209-212
6-Styryl-pyridine-2-carboxylic acid methyl ester	87-88
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	colorless oil
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol	227-229
Acetic acid 2-methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	102-103
2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridine	59-61
2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridine	83-85
2-[2-(2-Chloro-phenyl)-vinyl]-5-ethyl-pyridine	34-35
1-(6-Styryl-pyridin-2-yl)-ethanone	67-68
6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid ethyl ester	80-82
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid ethyl ester	70-72
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid; HCl salt	218-219
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid	150-151
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid	206-207
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester; HCl salt	237-238
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester	112-113
2-Methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	116-119
{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-methanol; HCl salt	230-231
6-Styryl-pyridine-2-carboxylic acid .tert.-butylamide	87-88
2-(2-Bromo-2-phenyl-vinyl)-6-methyl-pyridine; HCl salt	150-154
2-Methyl-6-phenylethynyl-pyridine; HCl salt	146-148
6-Styryl-pyridine-2-carboxylic acid hexylamide; HCl salt	118-125
6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid	219-221 dec
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid	168-170
2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridine	75-77
2-Methyl-6-[2-(3-trifluoromethyl-phenyl)-vinyl]-pyridine	44-45
(E)-6-[2-(4-pyridyl)vinyl]-2-Picoline	72-73
N,N-Diethyl-3-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide; HCl salt	227-228
N,N-Diethyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide; HCl salt	183-184
(E)-6-[2-(3-pyridyl)vinyl]-2-Picoline	yellowish oil
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid ethyl ester	colorless gum

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide; HCl salt	249-251
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide	160-161
2-[2-(3-Nitro-phenyl)-vinyl]-pyridine	127-128
6-Styryl-pyridine-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide	126-129
2-(6-Styryl-pyridin-2-yl)-propan-2-ol, HCl salt	171-174
2-Methyl-6-(2-thiophen-2-yl-vinyl)-pyridine, HCl salt	208-211
2-[2-(3-Chloro-phenyl)-vinyl]-pyridine	51-53
2-[2-(3-Cyano-phenyl)-vinyl]-pyridine	85-86
2-[2-(3-Bromo-phenyl)-vinyl]-6-methyl-pyridine	58-59
2-[2-(3-Bromo-phenyl)-2-fluoro-vinyl]-6-methyl-pyridine	58-59
2-[2-(3,5-Dimethylphenyl)-2-fluoro-vinyl]-6-methyl-pyridine	70-72
2-[2-(2,3-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine	colorless oil
2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridine	67-68
2-[2-(3-Chloro-phenyl)-1-methyl-vinyl]-pyridine	colorless oil
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-methanol	87-90
2-Methyl-6-[2-(3-trimethylsilanylethynyl-phenyl)-vinyl]-pyridine	yellowish oil
2-[2-(3,4-Difluoro-phenyl)-vinyl]-6-methyl-pyridine	61-62
2-[2-(3-Ethynyl-phenyl)-vinyl]-6-methyl-pyridine	yellowish oil
2-[2-(3,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine	yellowish oil
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridine	yellowish oil
2-[2-(3-Methoxy-phenyl)-vinyl]-6-methyl-pyridine	yellowish oil
2-Methyl-6-[2-(3-phenoxy-phenyl)-vinyl]-pyridine	yellowish oil
2-[2-(3-Benzyloxy-phenyl)-vinyl]-6-methyl-pyridine	68-69
2-[2-(2,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine	44-45
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid	230-233
(3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine	203-205
{6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanol	131-133
2-(3-Bromo-phenylethynyl)-6-methyl-pyridine	61-63
2-Methyl-6-{2-[3-(3-trifluoromethyl-phenoxy)-phenyl]-vinyl}-pyridine	yellowish oil
2-[2-(3,5-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine	43-45
2-[2-(3-Chloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine	52-53
Acetic acid 4-bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	yellowish oil
Acetic acid 3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	yellowish oil

2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridine	73-75
4-Bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	246-248
Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester	156-158
Acetic acid 6-[2-(3,5-dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester	159-161
Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-pyridin-3-yl ester	154-156
2-Methyl-6-(2-naphthalen-1-yl-vinyl)-pyridine	yellowish oil
2-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-vinyl]-6-methyl-pyridine	99-101
2-Methyl-6-(2-naphthalen-2-yl-vinyl)-pyridine	97-99
2-Methyl-6-(2-m-tolyl-vinyl)-pyridine	yellowish oil
2-{2-[3-(3,5-Dichloro-phenoxy)-phenyl]-vinyl}-6-methyl-pyridine	yellowish gum
2-[2-(3-Chloro-phenyl)-propenyl]-6-methyl-pyridine	yellowish oil
2-[2-(2,3-Dihydro-benzofuran-5-yl)-vinyl]-6-methyl-pyridine	88-90
2-[2-(4-Fluoro-phenyl)-vinyl]-6-methyl-pyridine	50-51
2-Methyl-6-(2-o-tolyl-vinyl)-pyridine	yellowish oil
2-Methyl-6-(2-p-tolyl-vinyl)-pyridine	85-86
2-Methyl-6-(2-p-tolyl-propenyl)-pyridine	yellowish oil
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine	126-129
(2,3-Dimethoxy-7-nitro-quinoxalin-5-ylmethyl)-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine	pale orange foam
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide	147
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide	156
2,2-Dimethyl-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-propionamide	166-168
Thiophene-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide	197 dec
Cyclohexanecarboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide	215
1-(4-Bromo-phenyl)-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea	197 dec
2-Methyl-6-[2-(4-nitro-phenyl)-vinyl]-pyridine	134-135
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine	147-148
2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol	218-220
6-[2-(3,5-Dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol	286 dec
2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-ol	240-242
2-[2-(6-Chloro-benzo[1,3]dioxol-5-yl)-vinyl]-6-methyl-pyridine	131-132
2-[2-(2,3-Difluoro-phenyl)-vinyl]-6-methyl-pyridine	55-56
2-[2-(3,4-Dichloro-phenyl)-propenyl]-6-methyl-pyridine	yellowish oil

2-[2-(3,5-Bis-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine	85-86
Acetic acid 2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	yellowish oil
2-Methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	118-120
2-Methyl-6-[2-(2,3,6-trifluoro-phenyl)-vinyl]-pyridine	59-62
2-[2-(4-Fluoro-3-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine	yellowish oil
2-Methyl-6-(2,3,6-trifluoro-phenylethynyl)-pyridine	93-94
Acetic acid 4-chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	yellowish oil
Acetic acid 2,6-di-.tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	127-128
3-(6-Methyl-pyridin-2-ylethynyl)-benzamide	187-189
Acetic acid 4-bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester	151-153
2-(6-Chloro-benzo[1,3]dioxol-5-ylethynyl)-6-methyl-pyridine	105-106 light brown crystals
2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine	127-129
2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-pyridine	111-113
5-Azido-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	143 dec
2-[2-(Pyridin-3-yl)ethynyl]-6-methyl-pyridine	light yellow crystals 60-61
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid	212-213
1-tert.-Butyl-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea	191-192
5-({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-methyl)-7-nitro-1,4-dihydro-quinoxaline-2,3-dione	250 dec
Tetrahydro-furan-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide	160-161
(1-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-2-phenyl-ethyl)-carbamic acid tert.-butyl ester	colorless foam
({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid tert.-butyl ester	colorless foam
Diethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine	217 dec
Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine	225 dec
Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine	183 dec
2-(2-Ethoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine	yellowish oil
2-(3,5-Difluoro-phenylethynyl)-6-methyl-pyridine	yellowish oil
2-(3-Fluoro-phenylethynyl)-6-methyl-pyridine	26-28
2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridine	56-57

2-[2-(3,4-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine	55-56
2-(3,4-Dichloro-phenylethynyl)-6-methyl-pyridine	73-74
2-(4-Ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine	61-62
2-(4-Fluoro-phenylethynyl)-6-methyl-pyridine	98-100
2-Methyl-6-.o.-tolylethynyl-pyridine	yellowish oil
2-(3,4-Difluoro-phenylethynyl)-6-methyl-pyridine	65-68
2-Methyl-6-[2-(2,3,5-trichloro-phenyl)-vinyl]-pyridine	80-82
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-ethanone	76-78
2-Methyl-6-(3-trifluoromethyl-phenylethynyl)-pyridine	35-37
2-Methyl-6-(3-nitro-phenylethynyl)-pyridine	99.5-102.5
6-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-2-methyl-pyridine	98-100
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-morpholin-4-yl-methanone	123-125
(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	207-210
N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid	201 dec
N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide	236-237 dec
({4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid .tert.-butyl ester	144-145 dec
1-tert.-Butyl-3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea	209 dec
{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine hydrochloride salt	161-162
Cyclohexylmethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine hydrochloride salt	178-179 dec
{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine	100
Cyclohexylmethyl-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine	106-107
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-3-phenyl-propionamide	102
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide	105
2-Amino-N-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide	217-219 dec
1-[1-({2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetyl)-piperidin-4-yl]-imidazolidin-2-one	amorphous foam
(1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-ethyl)-phosphonic acid dimethyl ester	orange amorphous solid
2-[2-(2-Methoxy-phenyl)-vinyl]-6-methyl-pyridine	129-130

2-(3-Ethoxy-4-fluoro-phenylethynyl)-6-methyl-pyridine	82-83
2-(3-Chloro-phenylethynyl)-6-methyl-pyridine	57-59
1-(3-Pyridin-2-ylethynyl-phenyl)-ethanone	48-51
4-Chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	256-260
4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	121-123
2-Methyl-6-.m.-tolylethynyl-pyridine	57-58
2-(2,5-Difluoro-phenylethynyl)-6-methyl-pyridine	49-50
2-(3,5-Dimethyl-phenylethynyl)-6-methyl-pyridine	yellowish oil
2-[2-(3,5-Dibromo-phenyl)-vinyl]-6-methyl-pyridine	68-70
2-Methyl-6-[2-(pyrimidin-5-yl)-ethynyl]-pyridine	110-112
(2-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-ethyl)-dimethyl-amine	165-167
Acetic acid 1-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-ethyl ester	
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol	250-251
3-(6-Methyl-pyridin-2-ylethynyl)-phenylamine	129-130
N-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-2-phenyl-acetamide	133-135 dec
Thiophene-2-carboxylic acid [3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-amide	156-157 dec
2-Methyl-6-(thiophen-2-ylethynyl)-pyridine	34-36
3-(6-Methyl-pyridin-2-ylethynyl)-benzoic acid ethyl ester	56-58
2-(3,5-Dibromo-phenylethynyl)-6-methyl-pyridine	100:101
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ylmethyl}-dimethyl-amine	227-229 dec
(3-{6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yloxy}-propyl)-dimethyl-	184-186
5-Azido-4-iodo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	red glass
2,6-Di-tert-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	126-127
1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanol	97-99
2-Methyl-6-[2-(pyrimidin-2-yl)-ethynyl]-pyridine	144-145
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-phenyl-methanone	99-100
6-(6-Methyl-pyridin-2-ylethynyl)-3,4-dihydro-1H-quinolin-2-one	189-191
2-(3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-isoindole-1,3-dione	101-103
3-Methoxy-6-methyl-2-.m.-tolylethynyl-pyridine	brown oil
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-4-nitro-phenyl ester	129-131
6-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one	160-165
2-Methyl-6-[2-(pyrazin-2-yl)-ethynyl]-pyridine	95-96

N-Methyl-N-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-acetamide	62-70
2-[2-(3,5-Bis-trifluoromethyl-phenyl)-1-ethoxy-vinyl]-6-methyl-pyridine	yellow oil
Acetic acid 2-phenylethynyl-pyridin-3-yl ester	brown oil
Acetic acid 6-methyl-2-.m.-tolylethynyl-pyridin-3-yl ester	brown oil
Acetic acid 4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenyl ester	91-93
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-4-nitro-phenol	275 dec
Dimethyl-[3-(2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine	yellowish oil
Dimethyl-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-amine	240-243
1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanone	56-58
2-(3-Fluoro-phenylethynyl)-quinoline	81-83
Acetic acid 2-methyl-6-styryl-pyridin-3-yl ester	93-96
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol	141-143
3-Ethoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol	175-178 dec
4-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol	184-187 dec
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-6-nitro-phenyl ester	105-110 dec
Dimethyl-[3-(6-methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine	yellow gum
2-Azido-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol	155-157 dec
Dimethyl-[3-(6-methyl-2-.m.-tolylethynyl-pyridin-3-yloxy)-propyl]-amine	yellowish oil
2-(3-Methanesulfonyl-phenylethynyl)-6-methyl-pyridine	108-110 dec
3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propylamine	186-189
4-Azido-.N.-(3-{2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-2-hydroxy-benzamide	99-102 dec
3-[3-(3-Dimethylamino-propoxy)-6-methyl-pyridin-2-ylethynyl]-benzonitrile	yellow gum
5-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one	133-134
2-Methyl-6-(2,3,5-trichloro-phenylethynyl)-pyridine	112-114
2-[2-(6-methyl-pyridin-3-yl)ethynyl]-6-methyl-pyridine	118-119
Dimethyl-{3-[6-methyl-2-(3-trifluoromethyl-phenylethynyl)-pyridin-3-yloxy]-propyl}-amine	yellow gum
2-[2-(6-methyl-pyridin-3-yl)ethynyl]-3-methoxy 6-methyl-pyridine hydrcchloride salt	198-199
2-Methyl-6-(5,6,7,8-tetrahydro-naphthalen-2-ylethynyl)-pyridine	50-51
3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine	151-153
(3-{4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-dimethyl-amine;	211-215

[6-(3-Fluoro-phenylethynyl)-pyridin-2-yl]-dimethyl-amine	brown oil
6'-(3-Fluoro-phenylethynyl)-3,4,5,6-tetrahydro-2.H.-[1,2']bipyridinyl	brown gum
{3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine	158-160
4-Azido-.N.-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-benzamide	161-163 dec
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid ethyl ester	105-110 dec
1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-3-ol	108-109
2-Ethynyl-6-(3-fluoro-phenylethynyl)-pyridine	89-90
3-Methyl-6-(6-methyl-pyridin-2-ylethynyl)-3H-benzooxazol-2-one	172-174
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid dimethylamide	154-157
1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-4-ol	amorphous white solid
5-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol	150-151 dec
5-[2-Bromo-2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol	158-159
5-[2-(6-Methyl-pyridin-2-yl)-E-vinyl]-2-nitro-phenol	171-173
5-[2-(6-Methyl-pyridin-2-yl)-Z-vinyl]-2-nitro-phenol	108-110
4-Azido-2-hydroxy-.N.-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide	180-182 dec
5-(3-Dimethylamino-propoxy)-6-phenylethynyl-pyridine-2-carboxylic acid ethyl ester	160-162
6-Methyl-2-styryl-pyrimidin-4-ol	221-225
2-Ethyl-6-(3-fluoro-phenylethynyl)-pyridine	brown oil
2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridine	74-76
2-Methyl-6-(3-trifluoromethoxy-phenylethynyl)-pyridine	<30; brown crystals
2-Methyl-6-(3-[1,2,4]triazol-1-yl-phenylethynyl)-pyridine	128-130
4-(6-Methyl-pyridin-2-ylethynyl)-phthalonitrile	138-140
2-Methyl-6-{2-[3-(1.H.-tetrazol-5-yl)-phenyl]-vinyl}-pyridine; compound with formic acid	234-240
3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine	97-100
{3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine	171-173
2-(3,5-Dimethyl-phenylethynyl)-3-methoxy-6-methyl-pyridine	yellowish oil
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-ol	251-253 Dec.

6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid ethyl ester	84-86
2-Azido-5-(6-methyl-pyridin-2-ylethynyl)-phenol	153-155 dec
6-(3,4-Dimethoxy-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester	149-152
2-(4-Methoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine	56-87
2-(3-Fluoro-phenylethynyl)-6-methoxy-pyridine	brown oil
2-(3-Fluoro-phenylethynyl)-5-methyl-pyridine	74-76
6-(3,5-Dichloro-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester	195-198
5-(3-Dimethylamino-propoxy)-6-(3,5-dimethyl-phenylethynyl)-pyridine-2-carboxylic acid ethyl ester	187-190
6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid	173-175
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanol	116-118
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone	138-140
2-(3-Fluoro-phenylethynyl)-6-methyl-nicotinic acid ethyl ester	brown oil
2-(3-Fluoro-phenylethynyl)-4,6-dimethyl-pyridine	brown oil
6-(3-Fluoro-phenylethynyl)-.N.-(5-methoxy-indan-2-ylmethyl)-2-methyl-nicotinamide	157-159
{[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-amino}-phenyl-acetic acid methyl ester	133-135
2-Methyl-6-(5-methyl-thiophen-2-ylethynyl)-pyridine	58-59
2-Methyl-6-(2,3,5-trimethyl-phenylethynyl)-pyridine	brown oil
3-{2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propan-1-ol	86-88
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-ylmethyl]-dimethyl-amine	220-222
2,2-Dimethyl-propionic acid 3-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl ester	yellowish oil
2-Azido-4-iodo-5-(6-methyl-pyridin-2-ylethynyl)-phenol	140 dec
6-Azido-2,4-diiodo-3-(6-methyl-pyridin-2-ylethynyl)-phenol	162 dec
4-Azido-2-hydroxy-5-iodo-.N.-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide	185 dec
Acetic acid 3-acetoxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-benzyl ester	brown oil
(Benzyl-{[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-acetyl}-amino)-acetic acid ethyl ester	brown oil
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid ethyl ester	76-77

3-[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propan-1-ol	72-74
[3-Hydroxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-phenyl]-methanol	115-117
(3-{2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine	yellowish gum
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-{6-[2-(3-fluoro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanone	156-158
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid	245-248
{6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-methanone	109-112
2-(3-Ethynyl-phenylethynyl)-6-methyl-pyridine	48-49
(3-{2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	207-210
(3-{2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	161-169
4-[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazine-1-carboxylic acid .tert.-butyl ester	97-99
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-piperazin-1-yl-methanone	250-252 dec
[4-(4-Azido-2-hydroxy-benzoyl)-piperazin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone	186-188 dec
(3-{2-[2-(2,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	170-176
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid ethyl ester	89-91
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid .tert.-butyl ester	94-96
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid	231 dec
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanol	143-146
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanone	156-158
3-Allyloxy-2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridine	105-106
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-morpholin-4-yl-methanone	114-116
Acetic acid 3-(6-methyl-pyridin-2-ylethynyl)-benzyl ester	brown oil
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-ylmethyl]-dimethyl-amine	209-212
(3-{2-[2-(3,5-Dichloro-phenyl)-propenyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	182-184
2-(3-Fluoro-phenylethynyl)-3-methoxy-6-methyl-pyridine	yellowish oil

(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	171-174
(4-Azido-2-hydroxy-5-iodo-phenyl)-{4-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazin-1-yl}-methanone	195-200 dec
4-Azido-.N.-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-5-iodo-benzamide	142-150 dec
4-(2-Pyridin-2-yl-vinyl)-benzoic acid ethyl ester	100-102
(3-{2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	159-171
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-methanol	43-45
6-(3-Fluoro-phenylethynyl)-nicotinic acid .tert.-butyl ester	96-98
(3-{2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt	174-177
2-(1-Bromo-2-phenyl-vinyl)-4-methyl-pyrimidine	yellow oil
6-(3-Fluoro-phenylethynyl)-nicotinic acid	223 dec.
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-pyridin-3-yl]-methanone	136.0-139.0
2-(2-.tert.-Butoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine	72.0-74.0
2-Methyl-6-[2-(2,4,5-trifluoro-phenyl)-vinyl]-pyridine	74-76
2-Methyl-6-[2-(2,3,4-trifluoro-phenyl)-vinyl]-pyridine	79-82
3-(6-Methyl-pyridin-2-ylethynyl)-phenol	142-144
2-Methyl-6-[2-(3,4,5-trifluoro-phenyl)-vinyl]-pyridine	74-76
2-(3-Methoxy-phenylethynyl)-6-methyl-pyridine	55-57
2-Methyl-6-(2,3,4-trifluoro-phenylethynyl)-pyridine	104-106

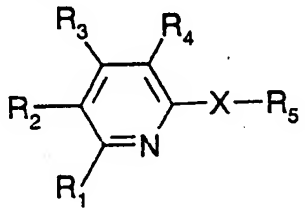
(dec = decomposition)

Claims:

1. A 2-arylalkenyl- , 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo- pyridine or a pharmaceutically acceptable salt thereof, for use in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

2. A 2-arylalkenyl- , 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo- pyridine or a pharmaceutically acceptable salt thereof, for use in the treatment of epilepsy, cerebral ischemia, ischemic diseases of the eye, muscle spasms, convulsions, pain, acute, traumatic and chronic degenerative processes of the nervous system and psychiatric diseases.

3. A compound of formula I



(I),

wherein

R_1 denotes hydrogen, lower alkyl,hydroxy-lower alkyl, lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R_2 denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 represents hydrogen, lower alkyl, carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy- lower alkyl, di- lower alkyl- aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy,

phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy,
X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and
R_5 denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-lower alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl-lower alkoxy-, halo- and/or trifluoromethyl-substituted,
in free form or in form of a photoaffinity ligand, a radioactive marker, an N-oxide or a pharmaceutically acceptable salt,

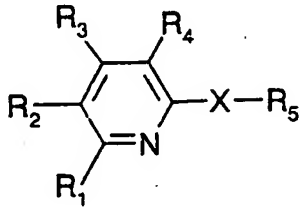
for use in the treatment of disorders associated with irregularities of the glutaminergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

4. The use of a compound according to claim 3, in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

5. The use of a compound according to claim 3, for the manufacture of a pharmaceutical composition designed for the treatment of disorders associated with irregularities of

the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

6. A compound of formula I



(I),

wherein

R_1 denotes hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R_2 denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 represents hydrogen, lower alkyl, carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy- lower alkyl, di- lower alkyl- aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy,

X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and

R_5 denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-low r alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy,

hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl-lower alkoxy-, halo- and/or trifluoromethyl-substituted,

in free form or in form of a photoaffinity ligand, a radioactive marker, an N-oxide or a pharmaceutically acceptable salt,

provided that, when R_3 is hydrogen,

a) in compounds of the formula I in which R_1, R_2 and R_4 are hydrogen, R_5 is different from phenyl, monohalophenyl, 2,4- and 3,4-dichlorophenyl, 3- and 4-trifluoromethylphenyl, methylphenyl, 3,4- and 2,5-dimethylphenyl, 4-isopropylphenyl, 3,5-di-tert.-butylphenyl, methoxyphenyl, 3,4-dimethoxyphenyl, 2,4,5- and 3,4,5-trimethoxyphenyl, hydroxyphenyl, 3,5-dihydroxyphenyl, 4-hydroxy-3,5-dimethyl-phenyl, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-phenyl, 4-hydroxy-(3-methyl-5-tert.-butyl-, 2- and 4-acetylaminophenyl, 3,5-diisopropyl- and 3,5-di-tert.-butyl)phenyl, 4-carboxy- and 4-ethoxycarbonylphenyl, 4-cyanophenyl, 3-methoxycarbonylphenyl, 3-carboxy-5-methoxy-phenyl, 2-pyridinyl, 5-chloro-2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene, or R_5 is different from phenyl, 4-methylphenyl, 4-methoxyphenyl, 4-bromophenyl and 2- and 4-chlorophenyl when X denotes 1,2-propylene attached to R_5 in 2-position, or R_5 is different from phenyl, 2- and 4-chlorophenyl and 3-methoxyphenyl when X denotes 1,2-propylene attached to R_5 in 1-position, or R_5 is different from 4-methoxyphenyl when X denotes 2,3-but-2-enylene or 1,2-but-1-enylene attached to R_5 in 2-position, or R_5 is different from 4-methoxyphenyl and 4-isopropyphenyl when X denotes 2,3-pent-2-enylene attached to R_5 in 3-position, or R_5 is different from phenyl, 4-methylphenyl, methoxyphenyl and 4-hydroxyphenyl when X denotes 3,4-hex-3-enylene;

b) in compounds of the formula I in which R_1 is methyl and R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 4-cyanophenyl, , 2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene;

c) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is carboxy, R_5 is different from phenyl, 3-methylphenyl, 4-methoxyphenyl and 4-bromophenyl when X denotes ethenylene;

d) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is methyl, R_5 is different from phenyl, 3-methoxy-, 4-methoxy- and 3,4-dimethoxyphenyl, 2-chloro- and 2,4-dichlorophenyl and 6-methyl-pyrid-2yl when X denotes ethenylene or R_5 is different from phenyl when X is 1,2-prop-1-enylene attached to R_5 in 2-position;

e) in compounds of the formula I wherein R_1 and R_2 are hydrogen and R_4 is 2-dimethylaminoethoxycarbonyl or 3-dimethylaminopropyloxycarbonyl, R_5 is different from 4-methoxyphenyl when X denotes ethenylene;

f) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is 2-dimethoxyethoxy, R_5 is different from phenyl, 4-methylphenyl and 4-methoxycarbonylphenyl when X denotes ethenylene;

g) R_5 is different from phenyl when R_1 and R_2 are hydrogen and R_4 is hydroxy or ethoxycarbonyl, or when R_1 and R_2 are hydrogen and R_4 is hydroxy, or when R_1 is methyl, R_2 is hydrogen and R_4 is methoxy, or R_1 is but-1-enyl, R_2 is hydrogen and R_4 is hydrogen, or R_1 is hydrogen and R_4 is 2-dimethoxyethoxy, and X is, in each case, ethenylene,

and provided that, when R_3 is hydrogen and X is ethynylene,

a') R_5 is different from phenyl, 2- and 4-nitrophenyl, 4-aminophenyl, 4-chlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 4-ethoxycarbonylphenyl, 5-formyl-2-methoxy-phenyl, 5-carboxy-2-methyo-phenyl and pyridyl when R_1, R_2 and R_4 are hydrogen;

b') in compounds of the formula I in which R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl. 6-methylpyridin-2-yl and 2-methoxyphenyl when R_1 is methyl, R_5 is different form 6-bromopyridin-2-yl when R_1 is bromo, and R_5 is different form 6-hexyloxypyridin-2-yl when R_1 denotes hexyloxy;

c') in compounds of the formula I wherein R_1 and R_4 are hydrogen, R_5 is different from phenyl, 4-aminophenyl and 4-propylphenyl when R_2 is methyl, R_5 is different from phenyl, 4-cyanophenyl and 4-pentylphenyl when R_2 is ethyl, R_5 is different form 3-cyano-4-ethoxy-phenyland 3-bromo-4-methoxy-phenyl when R_2 is butyl, R_5 is different from 4-methoxyphenyl and 4 butyloxyphenyl when R_2 is pentyl, R_5 is different form 4-ter.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl, 4-tert.-butyl-3-hydroxy-phenyl,and 4-hexyloxyphenyl when R_2 is carboxy, R_5 is different from phenyl when R_2 is methoxycarbonyl or methylcarbamoyl, R_4 is different form 3-tert.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl and 4-(4-methylpentyl)phenyl when R_2 is ethoxycarbonyl, and R_5 is different from 4-pentyloxyphenyl when R_2 is 2-methylbutyloxycarbonyl;

d') in compounds of the formula I wherein R_1 and R_2 are hydrogen, R_5 is different from phenyl when R_4 is hydroxy, methyl, ethyl, carboxy, methoxycarbonyl or carbamoyl.

7. A compound according to claim 6, wherein

X represents an optionally halo-substituted (C_{2-4})alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms,

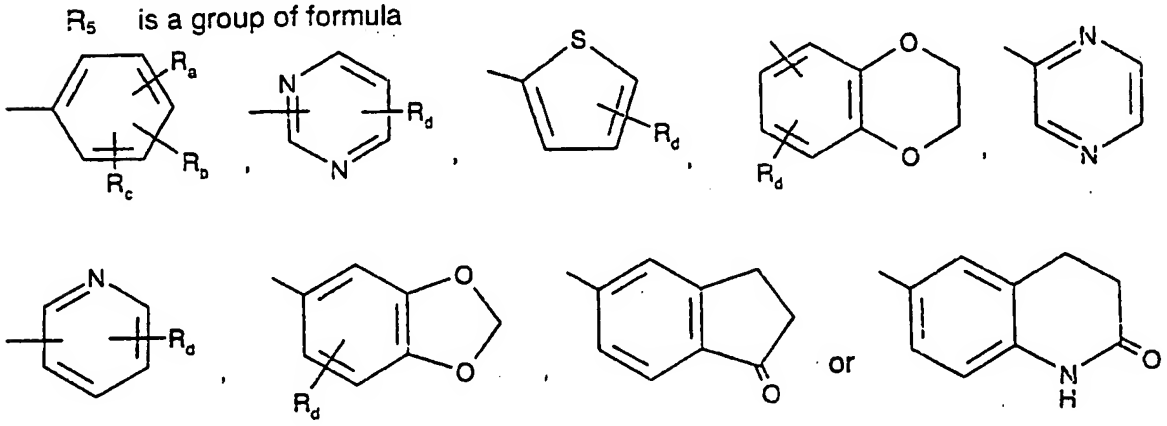
R_1 is hydrogen, (C_{1-4}) alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, cyano, ethynyl, carboxy, (C_{1-4})alkoxycarbonyl, di(C_{1-4})alkylamino, (C_{1-6})alkylaminocarbonyl, trifluoromethylphenylaminocarbonyl,

R_2 is hydrogen, hydroxy, (C_{1-4}) alkyl, hydroxy (C_{1-4}) alkyl, (C_{1-4}) alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4}) alkoxycarbonyl, di(C_{1-4})alkylamino(C_{1-4})alkanoyl, di(C_{1-4})alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 is hydrogen, (C_{1-4}) alkyl, carboxy, (C_{1-4})alkoxycarbonyl, (C_{1-4})alkylcarbamoyl, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 is hydrogen, hydroxy, (C_{1-4})alkoxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl, carboxy (C_{1-4})alkylcarbonyl, (C_{1-4})alkoxycarbonyl-(C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, di(C_{1-4})alkylamino(C_{1-4})alkoxy, m-hydroxy-p-azidophenylcarbonylamino(C_{1-4})alkoxy, and

R_5 is a group of formula



wher in

R_a and R_b independently are hydrogen, hydroxy, halogen, nitro, cyano, carboxy, (C_{1-4})alkyl, (C_{1-4})alkoxy, hydroxy(C_{1-4})alkyl, (C_{1-4})alkoxycarbonyl, (C_{2-7})alkanoyl,

(C_{2-5})alkanoyloxy, (C_{2-5})alkanoyloxy(C_{1-4})alkyl, trifluoromethyl, trifluoromethoxy, trimethylsilylethynyl, (C_{2-5})alkynyl, amino, azido, amino (C_{1-4})alkoxy, (C_{2-5})alkanoylamino(C_{1-4})alkoxy, (C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, (C_{1-4})alkylamino, di(C_{1-4})alkylamino, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, (C_{2-5})alkanoylamino, benzylcarbonylamino, (C_{1-4})alkylamino-carbonylamino, (C_{1-4})alkoxycarbonyl-aminocarbonylamino or (C_{1-4})alkylsulfonyl,

R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C_{1-4})alkyl, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxy or cyano, and

R_d is hydrogen, halogen or (C_{1-4})alkyl.

8. A compound according to claim 6, wherein

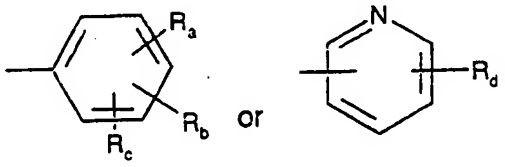
R_1 is hydrogen, (C_{1-4}) alkyl, (C_{1-4})alkoxy, cyano, ethynyl or di(C_{1-4})alkylamino,

R_2 is hydrogen, hydroxy, carboxy, (C_{1-4}) alkoxycarbonyl, di(C_{1-4})alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 is as defined in claim 7,

R_4 is hydrogen, hydroxy, carboxy, (C_{2-5})alkanoyloxy, (C_{1-4})alkoxycarbonyl, amino (C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkoxy, di(C_{1-4})alkylamino(C_{1-4})alkyl or hydroxy(C_{1-4})alkyl, and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, halogen, nitro, cyano, (C_{1-4})alkyl, (C_{1-4})alkoxy, trifluoromethyl, trifluoromethoxy or (C_{2-5})aikynyl, and

R_c and R_d are as defined in claim 7.

9. A compound according to claim 6, selected from

3-[2-(6-Methylpyridin-2-yl)-vinyl]-benzonitrile

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile

2-Methyl-6-[2-(pyridin-4-yl)-vinyl]-pyridine
2-Methyl-6-[2-(pyridin-3-yl)-vinyl]-pyridine
2-[2-(3-Bromophenyl)ethynyl]-6-methyl-pyridine
3-[2-(6-Methylpyridin-2-yl)ethynyl]-benzonitrile
2-Styryl-pyridin-3-ol
2-Methyl-6-[2-(3-nitro-phenyl)-vinyl]-pyridine
Acetic acid 6-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester
6-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester
2-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol
6-Methyl-2-styryl-pyridin-3-ol
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
(Z)-6-Methyl-2-styryl-pyridin-3-ol
2-[2-(2-Nitro-phenyl)-vinyl]-pyridine
Acetic acid 2-[2-(4-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
Acetic acid 6-[2-(4-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester
2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-[2-(4-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol
Acetic acid 6-methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester
6-Methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester
2-Methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
Acetic acid 6-[2-(3-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester
2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol
(Z)-(6-Styryl-pyridin-2-yl)-methanol
(E)-(6-Styryl-pyridin-2-yl)-methanol
Dimethyl-[3-(6-methyl-2-styryl-pyridin-3-yloxy)-propyl]-amine;
2-Methyl-6-styryl-pyridine 1-oxide
2-Styryl-pyridine 1-oxide
(E)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol
(Z)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol;
6-Styryl-pyridine-2-carbonitrile
2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridine

3-Methoxy-6-methyl-2-styryl-pyridine

6-Styryl-pyridine-2-carboxylic acid amide

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile

6-Styryl-pyridine-2-carboxylic acid;

6-Styryl-pyridine-2-carboxylic acid methyl ester

Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol

Acetic acid 2-methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(2-Chloro-phenyl)-vinyl]-5-ethyl-pyridine

1-(6-Styryl-pyridin-2-yl)-ethanone

6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid ethyl ester

2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid ethyl ester

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid;

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid

4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester

4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester

2-Methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol

{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-methanol;

6-Styryl-pyridine-2-carboxylic acid .tert.-butylamide

2-(2-Bromo-2-phenyl-vinyl)-6-methyl-pyridine;

6-Styryl-pyridine-2-carboxylic acid hexylamide;

6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid

2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid

2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridine

2-Methyl-6-[2-(3-trifluoromethyl-phenyl)-vinyl]-pyridine

(E)-6-[2-(4-Pyridyl)vinyl]-2-picoline

N,N-Diethyl-3-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide;

N,N-Diethyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide;

(E)-6-[2-(3-pyridyl)vinyl]-2-Picoline

{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid ethyl ester

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide;

4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide

2-[2-(3-Nitro-phenyl)-vinyl]-pyridine

6-Styryl-pyridine-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide

2-(6-Styryl-pyridin-2-yl)-propan-2-ol

2-Methyl-6-(2-thiophen-2-yl-vinyl)-pyridine

2-[2-(3-Cyano-phenyl)-vinyl]-pyridine

2-[2-(3-Bromo-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Bromo-phenyl)-2-fluoro-vinyl]-6-methyl-pyridine

2-[2-(3,5-Dimethylphenyl)-2-fluoro-vinyl]-6-methyl-pyridine

2-[2-(2,3-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Chloro-phenyl)-1-methyl-vinyl]-pyridine

{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-methanol

2-Methyl-6-[2-(3-trimethylsilanylethynyl-phenyl)-vinyl]-pyridine

2-[2-(3,4-Difluoro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Ethynyl-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Methoxy-phenyl)-vinyl]-6-methyl-pyridine

2-Methyl-6-[2-(3-phenoxy-phenyl)-vinyl]-pyridine

2-[2-(3-Benzyloxy-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(2,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine

{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid

(3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine

{6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanol

2-(3-Bromo-phenylethynyl)-6-methyl-pyridine

2-Methyl-6-{2-[3-(3-trifluoromethyl-phenoxy)-phenyl]-vinyl}-pyridine

2-[2-(3,5-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3-Chloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine

Acetic acid 4-bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

Acetic acid 3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridine

4-Bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol

Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester

Acetic acid 6-[2-(3,5-dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester

Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-pyridin-3-yl ester

2-Methyl-6-(2-naphthalen-1-yl-vinyl)-pyridine

2-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-vinyl]-6-methyl-pyridine

2-Methyl-6-(2-naphthalen-2-yl-vinyl)-pyridine

2-{2-[3-(3,5-Dichloro-phenoxy)-phenyl]-vinyl}-6-methyl-pyridine

2-[2-(3-Chloro-phenyl)-propenyl]-6-methyl-pyridine

2-[2-(2,3-Dihydro-benzofuran-5-yl)-vinyl]-6-methyl-pyridine

2-[2-(4-Fluoro-phenyl)-vinyl]-6-methyl-pyridine

2-Methyl-6-(2-o-tolyl-vinyl)-pyridine

2-Methyl-6-(2-p-tolyl-vinyl)-pyridine

2-Methyl-6-(2-p-tolyl-propenyl)-pyridine

3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine

(2,3-Dimethoxy-7-nitro-quinoxalin-5-ylmethyl)-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine

N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide

N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide

2,2-Dimethyl-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-propionamide

Thiophene-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide

Cyclohexanecarboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide

1-(4-Bromo-phenyl)-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea

2-Methyl-6-[2-(4-nitro-phenyl)-vinyl]-pyridine

4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine

2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol

6-[2-(3,5-Dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol

2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-ol

2-[2-(6-Chloro-benzo[1,3]dioxol-5-yl)-vinyl]-6-methyl-pyridine

2-[2-(2,3-Difluoro-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3,4-Dichloro-phenyl)-propenyl]-6-methyl-pyridine

2-[2-(3,5-Bis-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine

Acetic acid 2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

2-Methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol

2-Methyl-6-[2-(2,3,6-trifluoro-phenyl)-vinyl]-pyridine

2-[2-(4-Fluoro-3-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine

2-Methyl-6-(2,3,6-trifluoro-phenylethynyl)-pyridine

Acetic acid 4-chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

Acetic acid 2,6-di-.tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

3-(6-Methyl-pyridin-2-ylethynyl)-benzamide

Acetic acid 4-bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester

2-(6-Chloro-benzo[1,3]dioxol-5-ylethynyl)-6-methyl-pyridine

2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine

2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-pyridine

5-Azido-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol

2-[2-(Pyridin-3-yl)ethynyl]-6-methyl-pyridine

N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid

1-tert.-Butyl-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea

5-({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-methyl)-7-nitro-1,4-dihydro-quinoxaline-2,3-dione

Tetrahydro-furan-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide

(1-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-2-phenyl-ethyl)-carbamic acid tert.-butyl ester

({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid tert.-butyl ester

Diethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine

Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine

Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine

2-(2-Ethoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine

2-(3,5-Difluoro-phenylethynyl)-6-methyl-pyridine

2-(3-Fluoro-phenylethynyl)-6-methyl-pyridine

2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridine

2-[2-(3,4-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine

2-(3,4-Dichloro-phenylethynyl)-6-methyl-pyridine

2-(4-Ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine

2-(4-Fluoro-phenylethynyl)-6-methyl-pyridine

2-Methyl-6-o-tolylethynyl-pyridine

2-(3,4-Difluoro-phenylethynyl)-6-methyl-pyridine

2-Methyl-6-[2-(2,3,5-trichloro-phenyl)-vinyl]-pyridine

1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-ethanone

2-Methyl-6-(3-trifluoromethyl-phenylethynyl)-pyridine

2-Methyl-6-(3-nitro-phenylethynyl)-pyridine

6-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-2-methyl-pyridine

{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-morpholin-4-yl-methanone

(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine

N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid

N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide

({4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid .tert.-butyl ester

1-(tert.-Butyl-3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea

{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine hydrochloride salt
Cyclohexylmethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine hydrochloride salt
{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine
Cyclohexylmethyl-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-3-phenyl-propionamide
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide
2-Amino-N-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide
1-[1-({2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetyl)-piperidin-4-yl]-imidazolidin-2-one
(1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-ethyl)-phosphonic acid dimethyl ester
2-(3-Ethoxy-4-fluoro-phenylethynyl)-6-methyl-pyridine
2-(3-Chloro-phenylethynyl)-6-methyl-pyridine
1-(3-Pyridin-2-ylethynyl-phenyl)-ethanone
4-Chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2-(2,5-Difluoro-phenylethynyl)-6-methyl-pyridine
2-(3,5-Dimethyl-phenylethynyl)-6-methyl-pyridine
2-[2-(3,5-Dibromo-phenyl)-vinyl]-6-methyl-pyridine
3-(6-Methyl-pyridin-2-ylethynyl)-benzonitrile
2-Methyl-6-[2-(pyrimidin-5-yl)-ethynyl]-pyridine
(2-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-ethyl)-dimethyl-amine
Acetic acid 1-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-ethyl ester
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol
3-(6-Methyl-pyridin-2-ylethynyl)-phenylamine
.N.-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-2-phenyl-acetamide
Thiophene-2-carboxylic acid [3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-amide
2-Methyl-6-thiophen-2-ylethynyl-pyridine
3-(6-Methyl-pyridin-2-ylethynyl)-benzoic acid ethyl ester
2-(3,5-Dibromo-phenylethynyl)-6-methyl-pyridine
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ylmethyl}-dimethyl-amine
(3-{6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yloxy}-propyl)-dimethyl-
5-Azido-4-iodo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2,6-Di-tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanol
2-Methyl-6-[2-(pyrimidin-2-yl)-ethynyl]-pyridine
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-phenyl-methanone

6-(6-Methyl-pyridin-2-ylethynyl)-3,4-dihydro-1H-quinolin-2-one

2-(3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-isoindole-1,3-dione

3-Methoxy-6-methyl-2-.m.-tolylethynyl-pyridine

Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-4-nitro-phenyl ester

6-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one

2-Methyl-6-[2-(pyrazin-2-yl)-ethynyl]-pyridine

N-Methyl-.N.-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-acetamide

2-[2-(3,5-Bis-trifluoromethyl-phenyl)-1-ethoxy-vinyl]-6-methyl-pyridine

Acetic acid 2-phenylethynyl-pyridin-3-yl ester

Acetic acid 6-methyl-2-m-tolylethynyl-pyridin-3-yl ester

Acetic acid 4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenyl ester

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-4-nitro-phenol

Dimethyl-[3-(2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine

Dimethyl-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-amine

1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanone

2-(3-Fluoro-phenylethynyl)-quinoline

Acetic acid 2-methyl-6-styryl-pyridin-3-yl ester

4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol

3-Ethoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol

4-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol

Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-6-nitro-phenyl ester

Dimethyl-[3-(6-methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine

2-Azido-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol

Dimethyl-[3-(6-methyl-2-.m.-tolylethynyl-pyridin-3-yloxy)-propyl]-amine

2-(3-Methanesulfonyl-phenylethynyl)-6-methyl-pyridine

3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propylamine

4-Azido-N-(3-{2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-2-hydroxy-benzamide

3-[3-(3-Dimethylamino-propoxy)-6-methyl-pyridin-2-ylethynyl]-benzonitrile

5-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one

2-Methyl-6-(2,3,5-trichloro-phenylethynyl)-pyridine

2-[2-(6-methyl-pyridin-3-yl)ethynyl]-6-methyl-pyridine

Dimethyl-{3-[6-methyl-2-(3-trifluoromethyl-phenylethynyl)-pyridin-3-yloxy]-propyl}-amine

2-[2-(6-methyl-pyridin-3-yl)ethynyl]-3-methoxy 6-methyl-pyridine hydrochloride salt

2-Methyl-6-(5,6,7,8-tetrahydro-naphthalen-2-ylethynyl)-pyridine

3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine

(3-{4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-dimethyl-amine;

[6-(3-Fluoro-phenylethynyl)-pyridin-2-yl]-dimethyl-amine

6'-(3-Fluoro-phenylethynyl)-3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl

{3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine

4-Azido-N-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-benzamide

1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid ethyl ester

1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-3-ol

2-Ethynyl-6-(3-fluoro-phenylethynyl)-pyridine

3-Methyl-6-(6-methyl-pyridin-2-ylethynyl)-3H-benzooxazol-2-one

1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid

1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid dimethylamide

1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-4-ol

5-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol

5-[2-Bromo-2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol

5-[2-(6-Methyl-pyridin-2-yl)-E-vinyl]-2-nitro-phenol

5-[2-(6-Methyl-pyridin-2-yl)-Z-vinyl]-2-nitro-phenol

4-Azido-2-hydroxy-N-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide

5-(3-Dimethylamino-propoxy)-6-phenylethynyl-pyridine-2-carboxylic acid ethyl ester

6-Methyl-2-styryl-pyrimidin-4-ol

2-Ethyl-6-(3-fluoro-phenylethynyl)-pyridine

2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridine

2-Methyl-6-(3-trifluoromethoxy-phenylethynyl)-pyridine

2-Methyl-6-(3-[1,2,4]triazol-1-yl-phenylethynyl)-pyridine

4-(6-Methyl-pyridin-2-ylethynyl)-phthalonitrile

2-Methyl-6-{2-[3-(1H-tetrazol-5-yl)-phenyl]-vinyl}-pyridine; compound with formic acid

3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine

{3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine

2-(3,5-Dimethyl-phenylethynyl)-3-methoxy-6-methyl-pyridine

2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-ol

6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid ethyl ester

2-Azido-5-(6-methyl-pyridin-2-ylethynyl)-phenol

6-(3,4-Dimethoxy-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester

2-(4-Methoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine

2-(3-Fluoro-phenylethynyl)-6-methoxy-pyridine

2-(3-Fluoro-phenylethynyl)-5-methyl-pyridine

6-(3,5-Dichloro-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester

5-(3-Dimethylamino-propoxy)-6-(3,5-dimethyl-phenylethynyl)-pyridine-2-carboxylic acid ethyl ester

6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid

[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanol

[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone

2-(3-Fluoro-phenylethynyl)-6-methyl-nicotinic acid ethyl ester

2-(3-Fluoro-phenylethynyl)-4,6-dimethyl-pyridine

6-(3-Fluoro-phenylethynyl)-.N.-(5-methoxy-indan-2-ylmethyl)-2-methyl-nicotinamide

{[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-amino}-phenyl-acetic acid methyl ester

2-Methyl-6-(5-methyl-thiophen-2-ylethynyl)-pyridine

2-Methyl-6-(2,3,5-trimethyl-phenylethynyl)-pyridine

3-{2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propan-1-ol

[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-ylmethyl]-dimethyl-amine

2,2-Dimethyl-propionic acid 3-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl ester

2-Azido-4-iodo-5-(6-methyl-pyridin-2-ylethynyl)-phenol

6-Azido-2,4-diiodo-3-(6-methyl-pyridin-2-ylethynyl)-phenol

4-Azido-2-hydroxy-5-iodo-.N.-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide

Acetic acid 3-acetoxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-benzyl ester

(Benzyl-{[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-acetyl}-amino)-acetic acid ethyl ester

2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid ethyl ester

3-[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propan-1-ol

[3-Hydroxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-phenyl]-methanol

(3-{2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine

[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-{6-[2-(3-fluoro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanone

2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid

{6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-methanone

2-(3-Ethynyl-phenylethynyl)-6-methyl-pyridine

(3-{2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
(3-{2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
4-[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazine-1-carboxylic acid tert.-butyl ester
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-piperazin-1-yl-methanone
[4-(4-Azido-2-hydroxy-benzoyl)-piperazin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone
(3-{2-[2-(2,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid ethyl ester
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid .tert.-butyl ester
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanol
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanone
3-Allyloxy-2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridine
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-morpholin-4-yl-methanone
Acetic acid 3-(6-methyl-pyridin-2-ylethynyl)-benzyl ester
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-ylmethyl]-dimethyl-amine
(3-{2-[2-(3,5-Dichloro-phenyl)-propenyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(3-Fluoro-phenylethynyl)-3-methoxy-6-methyl-pyridine
(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-yloxy}-propyl)-dimethyl-amine
(4-Azido-2-hydroxy-5-iodo-phenyl)-{4-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazin-1-yl}-methanone
4-Azido-N-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-5-iodo-benzamide
4-(2-Pyridin-2-yl-vinyl)-benzoic acid ethyl ester
(3-{2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-methanol
6-(3-Fluoro-phenylethynyl)-nicotinic acid tert.-butyl ester
(3-{2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(1-Bromo-2-phenyl-vinyl)-4-methyl-pyrimidine
6-(3-Fluoro-phenylethynyl)-nicotinic acid
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-pyridin-3-yl]-methanone
2-(2-.tert.-Butoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-[2-(2,4,5-trifluoro-phenyl)-vinyl]-pyridine
2-Methyl-6-[2-(2,3,4-trifluoro-phenyl)-vinyl]-pyridine

3-(6-Methyl-pyridin-2-ylethynyl)-phenol
2-Methyl-6-[2-(3,4,5-trifluoro-phenyl)-vinyl]-pyridine
2-(3-Methoxy-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-(2,3,4-trifluoro-phenylethynyl)-pyridine
and pharmaceutically acceptable salts thereof.

10. (3-{2-[2-trans-(3,5-dichlorophenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethylamine in free form or in form of a pharmaceutically acceptable salt.

11. A pharmaceutical composition comprising as pharmaceutical active ingredient, together with customary pharmaceutical excipients, a compound according to any of claims 6 to 10, in free form or in form of a pharmaceutically acceptable salt.

12. A method of treating disorders mediated full or in part by mGluR1 or mGluR5, which method comprises administering to a warm-blooded organism in need of such treatment a therapeutically effective amount of an 2-arylalkenyl- , 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo- pyridine or a pharmaceutically acceptable salt thereof.

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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : C07D 213/65, A61K 31/44, C07D 213/80, 401/12, 401/06 | A3

(11) International Publication Number: WO 99/02497

(43) International Publication Date: 21 January 1999 (21.01.99)

(21) International Application Number: PCT/EP98/04266

(22) International Filing Date: 9 July 1998 (09.07.98)

(30) Priority Data:

08/891,691	11 July 1997 (11.07.97)	US
08/890,689	11 July 1997 (11.07.97)	US

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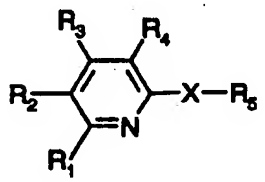
(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(88) Date of publication of the international search report:
1 April 1999 (01.04.99)

(54) Title: PYRIDINE DERIVATIVES



(I)

(57) Abstract

Compounds of the formula (I), wherein X and R_1 to R_5 are as defined in the description, are useful for treating disorders mediated full or in part by mGluR5.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/04266

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D213/65 A61K31/44 C07D213/80 C07D401/12 C07D401/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 334 119 A (BOEHRINGER INGELHEIM PHARMA) 27 September 1989 see page 16; claim 1 ---	1-3,6-11
X	DOWELL R.I.; HALES, N. H., TUCKER H.: "Novel inhibitors of prolyl 4-hydroxylase. Part 4. Pyridine-2-carboxylic acid analogues with alternative 2-substituents" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, vol. 28, no. 6, 1993, pages 513-516, XP002087215 see page 514; example 19 --- -/--	1-3,6-11

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
9 December 1998	07.01.99

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Lauro, P

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/04266

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LAZER E. S. ET AL: "Effect of structure on potency and selectivity in 2,6-disubstituted 4-(2-arylethenyl)phenol lipoxygenase inhibitors" JOURNAL OF MEDICINAL CHEMISTRY, vol. 33, no. 7, 1990, pages 1892-98, XP002087216 see page 1894; example 54 ---	1-3,6-11
X	BAHNER, C. T. ET AL. : "Di- and tri-methoxystyryl derivatives of heterocyclic nitrogen compounds" ARZNEIM. FORSCH. / DRUG RES., vol. 31, no. 3, 1981, pages 404-6, XP002087217 see page 405; examples 6-8 ---	1-3,6-11
X	HONMA Y; HANAMOTO K; HASHIYAMA T; SEKINE Y; TAKEDA M; ONO Y: "Antiallergic agents. 3. N-(1H-tetrazol-5-yl)-2-pyridinecarboxamides" JOURNAL OF MEDICINAL CHEMISTRY, vol. 27, no. 2, 1984, pages 125-128, XP002087218 see example 9 ---	1-3,6-11
X	MORI M ET AL: "THE NEMATICIDAL ACTIVITY OF ACETYLENE COMPOUNDS" AGRICULTURAL AND BIOLOGICAL CHEMISTRY, vol. 46, no. 1, 1982, pages 309-311, XP000645051 see example 14; table III ---	1-3,6-10
X	D. JERCHEL; H. E. HECK: "Kondensation von Methylpyridinen mit Benzaldehyd" JUSTUS LIEBIGS ANN. CHEM., vol. 613, 1958, pages 171-177, XP002087219 see page 174; example III ---	1-3,6-10
X	SADAO ARAI ET AL.: "Synthesis and reactions of methylbenzo[c]quinolizinium salts" JOURNAL OF HETEROCYCLIC CHEMISTRY, XP002087220 see example 4 ---	1-3,6-10
X	B.D. SHAW; E.A. WAGSTAFF: "The nitration of beta-phenylethylpyridines and related compounds" JOURNAL OF THE CHEMICAL SOCIETY, XP002087221 * see compounds of formula (II) and (III)* --- -/--	1-3,6-10

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 98/04266

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 19049 A (CIBA GEIGY AG ;SANDOZ AG (DE); NOVARTIS ERFINDUNGEN VERWALTUN (AT)) 29 May 1997 see page 1-5 ---	1-3,5-11
A	WO 97 05109 A (NOVONORDISK AS ;LUNDBECK JANE MARIE (DK); KANSTRUP ANDERS (DK)) 13 February 1997 see page 13-17; claim 1 -----	1-3,5-11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 98/04266

Box I Observations where certain claims were found unsearchable (Continuation f item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 4,12
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 4 and 12 are directed to a method for treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compounds/compositions

2. [X] Claims Nos.: -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the huge number of documents which disclose the compounds claimed in claims 1-3, 6-11, and which could not all be cited in the search report, the search is to be considered incomplete as far as the claims directed to compounds per se and their pharmaceutical compositions are concerned. The compounds in the form of photoaffinity ligands and radioactive markers have not been searched since no support in the description could be found. Claim 5 has been searched completely.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 98/04266

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0334119 A	27-09-1989	AU 628324 B	17-09-1992
		AU 3151489 A	21-09-1989
		DD 283602 A	17-10-1990
		DE 68907095 T	05-01-1994
		DK 134489 A	22-09-1989
		ES 2056983 T	16-10-1994
		FI 891295 A	22-09-1989
		JP 2004729 A	09-01-1990
		MX 9203255 A	01-07-1992
		PH 26928 A	03-12-1992
		PT 90066 A,B	10-11-1989
WO 9719049 A	29-05-1997	IT MI952383 A	19-05-1997
		AU 7627496 A	11-06-1997
WO 9705109 A	13-02-1997	AU 6514296 A	26-02-1997
		EP 0843660 A	27-05-1998
		US 5696148 A	09-12-1997